

RAW SEQUENCE LISTING
PATENT APPLICATION US/08/376,327A

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#5

DATE: 10/31/95
TIME: 14:34:39

INPUT SET: S6965.raw

This Raw Listing contains the General
Information Section and up to the first 5 pages.

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SEQUENCE LISTING

1
2
3 (1) General Information:
4
5 (i) APPLICANT: Thomson, James A
6
7 (ii) TITLE OF INVENTION: Primate Embryonic Stem Cells
8
9 (iii) NUMBER OF SEQUENCES: 6
10
11 (iv) CORRESPONDENCE ADDRESS:
12 (A) ADDRESSEE: Quarles & Brady
13 (B) STREET: 1 South Pinckney Street
14 (C) CITY: Madison
15 (D) STATE: WI
16 (E) COUNTRY: US
17 (F) ZIP: 53703
18
19 (v) COMPUTER READABLE FORM:
20 (A) MEDIUM TYPE: Floppy disk
21 (B) COMPUTER: IBM PC compatible
22 (C) OPERATING SYSTEM: PC-DOS/MS-DOS
23 (D) SOFTWARE: PatentIn Release #1.0, Version #1.30
24
25 (vi) CURRENT APPLICATION DATA:
26 (A) APPLICATION NUMBER: US 08/376,327
27 (B) FILING DATE: 20-JAN-1995
28 (C) CLASSIFICATION:
29
30 (viii) ATTORNEY/AGENT INFORMATION:
31 (A) NAME: Seay, Nicholas J
32 (B) REGISTRATION NUMBER: 27,386
33 (C) REFERENCE/DOCKET NUMBER: 960296.92905
34
35 (ix) TELECOMMUNICATION INFORMATION:
36 (A) TELEPHONE: 608-251-5000
37 (B) TELEFAX: 608-251-9166
38
39
40 (2) INFORMATION FOR SEQ ID NO:1:
41
42 (i) SEQUENCE CHARACTERISTICS:
43 (A) LENGTH: 25 base pairs
44 (B) TYPE: nucleic acid
45 (C) STRANDEDNESS: double
46 (D) TOPOLOGY: linear

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RAW SEQUENCE LISTING
PATENT APPLICATION US/08/376,327ADATE: 10/31/95
TIME: 14:34:44

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47
48 (ii) MOLECULE TYPE: DNA (genomic)
49
50
51
52
53 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
54
55 GCTGGATTGT CTGCAGGATG GGGAA 25
56
57 (2) INFORMATION FOR SEQ ID NO:2:
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59 (i) SEQUENCE CHARACTERISTICS:
60 (A) LENGTH: 25 base pairs
61 (B) TYPE: nucleic acid
62 (C) STRANDEDNESS: double
63 (D) TOPOLOGY: linear
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65 (ii) MOLECULE TYPE: DNA (genomic)
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68
69
70 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:
71
72 TCCCCTGAAG AAAATTGGTT AAAAT 25
73
74 (2) INFORMATION FOR SEQ ID NO:3:
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76 (i) SEQUENCE CHARACTERISTICS:
77 (A) LENGTH: 29 base pairs
78 (B) TYPE: nucleic acid
79 (C) STRANDEDNESS: double
80 (D) TOPOLOGY: linear
81
82 (ii) MOLECULE TYPE: DNA (genomic)
83
84
85
86
87 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:
88
89 GGATCCACCG TCAACACCAC CATCTGTGC 29
90
91 (2) INFORMATION FOR SEQ ID NO:4:
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93 (i) SEQUENCE CHARACTERISTICS:
94 (A) LENGTH: 30 base pairs
95 (B) TYPE: nucleic acid
96 (C) STRANDEDNESS: double
97 (D) TOPOLOGY: linear
98
99 (ii) MOLECULE TYPE: DNA (genomic)

RAW SEQUENCE LISTING
PATENT APPLICATION US/08/376,327ADATE: 10/31/95
TIME: 14:34:49

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100
101
102
103
104 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:
105
106 GGATCCACAG GTCAAAGGGT GGCCTTGGG 30
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108 (2) INFORMATION FOR SEQ ID NO:5:
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110 (i) SEQUENCE CHARACTERISTICS:
111 (A) LENGTH: 30 base pairs
112 (B) TYPE: nucleic acid
113 (C) STRANDEDNESS: double
114 (D) TOPOLOGY: linear
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116 (ii) MOLECULE TYPE: DNA (genomic)
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120
121 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:
122
123 GGGAATTCGC AGTTACTGAG AACTCACAAG 30
124
125 (2) INFORMATION FOR SEQ ID NO:6:
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127 (i) SEQUENCE CHARACTERISTICS:
128 (A) LENGTH: 30 base pairs
129 (B) TYPE: nucleic acid
130 (C) STRANDEDNESS: double
131 (D) TOPOLOGY: linear
132
133 (ii) MOLECULE TYPE: DNA (genomic)
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136
137
138 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:
139
140 GGGAATTCGA AGCATGTCAA AGTGGTATGG 30
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Claims 1-11 are currently pending in the instant application and have been examined on the merits. Claims 1-8 appear to be drawn to a purified preparation of primate embryonic stem cells wherein stem cells have certain morphological characteristics. Claims 9-10 appear to be drawn to a method of isolating primate embryonic stem cells. The method comprises isolating the blastocyst, isolating cells from the ICM, plating the ICM cells on an embryonic fibroblasts, dissociating the ICM derived cells, replating the ICM derived cells on an embryonic feeder layer, selecting the embryonic cells and culturing the selected cells. Claim 11 is drawn to a primate embryonic stem cell line isolated by the claimed method.

Claims 1-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite for recitation of "capable of proliferation in vitro culture." The syntax is awkward and confusing. Applicants may consider reciting "which is capable of proliferating in an *in vitro* culture."

Claims 1 and 3 are rendered vague and indefinite for not defining the metes and bounds of the phrase a "normal karyotype(s)." It is unclear which characteristics are considered normal.

Claim 1 is rendered indefinite for recitation of "differentiate to derivatives." It appears that applicants intended to recite "differentiate into derivatives."

Claim 9 is rejected for recitation "isolating a primate blastocyst; . . . the blastocyte of (a)." Step (a) does not recite "blastocyte" but rather "blastocyst", thus, the recitation of "blastocyte" in step (b) lacks proper antecedent basis.

Claim 10 is rejected for recitation of "isolated cells or a fibroblast feeder layer"
It appears that applicants intended to recite "isolated cells **on** a fibroblast feeder layer"
(emphasis added).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form
5 the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described
10 in a printed publication in this or a foreign country, before the invention thereof by the
applicant for a patent.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all
obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or
15 described as set forth in section 102 of this title, if the differences between the subject
matter sought to be patented and the prior art are such that the subject matter as a whole
would have been obvious at the time the invention was made to a person having ordinary
skill in the art to which said subject matter pertains. Patentability shall not be negated
by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under
20 subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this
section where the subject matter and the claimed invention were, at the time the invention
was made, owned by the same person or subject to an obligation of assignment to the
same person.

Claims 1-8 and 11 are rejected under 35 U.S.C. § 102(a) as anticipated by or, in the
25 alternative, under 35 U.S.C. § 103 as obvious over Nation/World (Nov. 4, 1994).

Nation/World discloses isolated embryonic stem cells from rhesus monkeys and
marmosets. Nation/World indicates that these cells are the parent cells of the many tissues in
the primates body, and can be induced to grow into any kind of tissue.

Nation/World does not specifically mention the specific morphological characteristics which are indicated in the claims, however, these characteristics are inherent features of the particular type of cell—rhesus monkey embryonic stem cells. Furthermore, the method of obtaining the cell line does not appear to patentably distinguish the embryonic stem cells from the prior art.

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not applicants' isolated embryonic stem cells differ and, if so, to what extent, from the cells discussed in the references. Accordingly, in as much as the examiner has established that the prior art cells, which are obtained from the same source, rhesus monkeys, as that claimed, likewise shares the property of being able to be induced to grow into any kind of tissue, she has reasonably demonstrated a reasonable likelihood/possibility that the compared cells are either identical or sufficiently similar that whatever differences exist are not patentably significant. Therefore, the burden of establishing non-obviousness by objective evidence shifted to applicants.

Accordingly, the claimed invention would have been at least *prima facie* obvious, if not anticipated, by one of ordinary skill in the art at the time the claimed invention was made, especially in the absence of sufficient, clear and convincing evidence to the contrary.

Claims 1-8 and 11 are rejected under 35 U.S.C. § 102(a) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as being obvious over Bongso et al (Human Reproduction) or Bongso et al. (Theriogenology).

Both Bongso et al. references teach isolated preparations of human embryonic stem (ES)

cells. Humans are classified as primates. The ES cells are isolated from the inner cell mass by culturing the cells on various feeder layers. The cells were alkaline phosphatase positive.

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not applicants' isolated embryonic stem cells differ and, if so, to what extent, from the cells discussed in the references. Accordingly, in as much as the examiner has established that the prior art cells, which are obtained from the same source, primates, as that claimed, likewise shares the property of being alkaline phosphatase positive, she has reasonably demonstrated a reasonable likelihood/possibility that the compared cells are either identical or sufficiently similar that whatever differences exist are not patentably significant. Therefore, the burden of establishing non-obviousness by objective evidence shifted to applicants.

Accordingly, the claimed invention would have been at least *prima facie* obvious, if not anticipated, by one of ordinary skill in the art at the time the claimed invention was made, especially in the absence of sufficient, clear and convincing evidence to the contrary.

Claims 9-11 are rejected under 35 U.S.C. § 103 as being unpatentable over Piedrahata et al. (Theriogenology).

The claims are drawn to a method of isolating primate ES cells. ICM cells are isolated from the blastocyst, the ICM cells are then plated on embryonic fibroblast feeder layers, dissociated, replated onto embryonic feeder layers and the selected. The selected ES cells are then maintained on a fibroblast feeder layer.

Piedrahata et al. teach a method of isolating murine, porcine and ovine embryonic stem cells. The blastocysts were isolated and then the cells from the ICM were isolated. These ICM

cells were plated on embryonic fibroblast feeder layers (STO feeder layers). After plating the growing ICM cells were dissociated and replated onto fresh feeder layers. ES cells were then selected based on a large nucleus and prominent nucleoli. These selected cells were then cultured on fresh feeder layer in order to prevent differentiation.

5 The only apparent difference between the method of Piedrahata et al. and that of the instant claims is that the claims isolate primate ES cells whereas Piedrahata et al. isolates murine, porcine and ovine ES cells. However, one of ordinary skill in the art would have a reasonable expectation of success in isolating primate ES using the same method as taught by Piedrahata et al for isolating murine, porcine or ovine ES cells.

10 As decided in In re O'Farrel, 7 USPQ 2d 1673 (Fed. Cir. 1988), obviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious. In re Merck & Co., 800 F.2d at 1098, 231 USPQ at 380; Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1461, 221 USPQ 481, 488 (Fed. Cir. 1984); In re Papesch, 315 F.2d 381, 386-387, 137 USPQ 43, 47-48 (CCPA 1963). For obviousness under 35 U.S.C. 103, all that is required is a reasonable expectation of success. In re Longi, 759 F.2d 887, 897, 225 USPQ 645, 651-652 (Fed. Cir. 1985); In re Clinton, 527 F.2d 1226, 1228, 188
15 USPQ 365, 367 (CCPA 1976).
20

Accordingly, the claimed invention would have been *prima facie* obvious to one of


ordinary skill in the art at the time the claimed invention was made, especially in the absence of sufficient, clear and convincing evidence to the contrary.

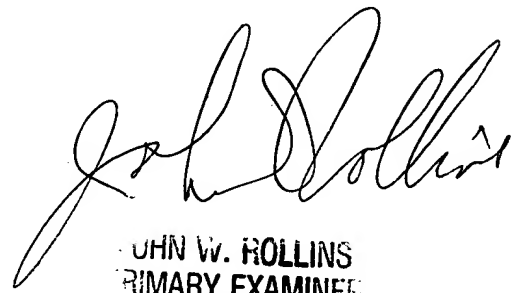
No claim is allowed.

5 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Susan M. Dadio whose telephone number is (703) 308-2392.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

10


Susan M. Dadio
December 28, 1995


JOHN W. ROLLINS
PRIMARY EXAMINER
ART UNIT 180